JAMA | Review

Diagnosis, Risk Stratification, and Treatment of Pericarditis
A Review

Paul C. Cremer, MD, MS; Allan L. Klein, MD; Massimo Imazio, MD

IMPORTANCE Pericarditis accounts for up to 5% of emergency department visits for nonischemic chest pain in North America and Western Europe. With appropriate treatment, 70% to 85% of these patients have a benign course. In acute pericarditis, the development of constrictive pericarditis (<0.5%) and pericardial tamponade (<3%) can be life-threatening.

OBSERVATIONS Acute pericarditis is diagnosed with presence of 2 or more of the following: sharp, pleuritic chest pain that worsens when supine (≈90%); new widespread electrocardiographic ST-segment elevation and PR depression (≈25%-50%); a new or increased pericardial effusion that is most often small (≈60%); or a pericardial friction rub (<30%). In North America and Western Europe, the most common causes of acute pericarditis are idiopathic or viral, followed by pericarditis after cardiac procedures or operations. Tuberculosis is the most common cause in endemic areas and is treated with antituberculosis therapy, with corticosteroids considered for associated constrictive pericarditis. Treatment of acute idiopathic and pericarditis after cardiac procedures or operations involves use of high-dose nonsteroidal anti-inflammatory drugs (NSAIDs), with doses tapered once chest pain has resolved and C-reactive protein level has normalized, typically over several weeks. These patients should receive a 3-month course of colchicine to relieve symptoms and reduce the risk of recurrence (37.5% vs 16.7%; absolute risk reduction, 20.8%). With a first recurrence of pericarditis, colchicine should be continued for at least 6 months. Corticosteroids are often used if pericarditis does not improve with NSAIDs and colchicine. In certain patients with multiple recurrences, which can occur for several years, interleukin 1 (IL-1) blockers have demonstrated efficacy and may be preferred to corticosteroids.

CONCLUSIONS Acute pericarditis is a common cause of nonischemic chest pain. Tuberculosis is the leading cause of pericarditis in endemic areas and is treated with antitubercular therapy. In North America and Western Europe, pericarditis is typically idiopathic, develops after a viral infection, or develops following cardiac procedures or surgery. Treatment with NSAIDs and colchicine leads to a favorable prognosis in most patients, although 15% to 30% of patients develop recurrence. Patients with multiple recurrent pericarditis can have a disease duration of several years or more, are often treated with corticosteroids, and IL-1 blockers may be used for selected patients as steroid-sparing therapy.

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The incidence of pericarditis in the general population is estimated at 27.7 cases per 100 000 per year, and pericarditis represents up to 5% of emergency visits for nonischemic chest pain in North American and Western Europe.[1] With appropriate recognition and treatment, 70% to 85% of these patients have a benign course with resolution of symptoms and no recurrence when treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine.[2,3] Recurrent pericarditis is defined by return of pericarditis symptoms after clinical remission of at least 4 to 6 weeks. Incessant pericarditis is defined by symptoms lasting at least 4 to 6 weeks but less than 3 months without remission.[1] After a first recurrence, subsequent episodes of pericarditis may occur in up to 50%,[1,4] and these patients have a markedly impaired health-related quality of life due to chest pain, impaired physical and mental health, sleep disturbance, and decreased work activity.[5] For patients with autoimmune disease–associated pericarditis, the risk of further recurrence during a median 35 months of follow-up was 88% compared with a rate of 69% in those with idiopathic pericarditis.[6] Patients with acute idiopathic pericarditis rarely develop constrictive pericarditis (<0.5%) or pericardial tamponade (<3%),[7,8] but these complications can be life-threatening and are more common in patients with bacterial (≈33%) or tuberculous (≈20%) pericarditis.[1] In addition, about 20% of patients with incessant pericarditis develop constrictive pericarditis.[9] This review focuses on the diagnostic evaluation of an individual with suspected initial or recurrent pericarditis, current recommended treatments, and prognosis (**Box**).

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Box. Common Questions About Pericarditis

What Are the Most Common Causes of Pericarditis?
In North America and Western Europe, the most common causes of pericarditis are idiopathic or viral, followed by pericarditis after cardiac procedures or operations. In areas where tuberculosis is endemic, tuberculosis is the most common cause of pericarditis.

What Are the Initial Treatments for Acute Pericarditis?
Treatment is directed at the underlying cause for certain conditions, such as tuberculous pericarditis and pericarditis related to a systemic autoimmune disease. For patients with idiopathic or viral pericarditis, or pericarditis after a cardiac procedure or surgery, initial treatment is high-dose NSAIDs and colchicine.

What Treatments Are Available for Recurrent Pericarditis?
Prednisone (0.25-0.5 mg/kg) is used in patients with recurrent pericarditis who have symptoms refractory to NSAIDs and colchicine. In certain patients, IL-1 blockers are preferred to corticosteroid therapy.

Abbreviations: IL-1, interleukin 1; NSAID, nonsteroidal anti-inflammatory drug.

Methods

We searched PubMed for English-language studies published from January 1, 2014, through May 5, 2024, with the heading *pericarditis*, which yielded 1992 initial results. We also manually searched the references of selected articles, and articles were selected for inclusion based on agreement by the authors. We included 53 articles, consisting of 2 guidelines, 15 clinical trials, 4 multicenter registries, 21 observational studies, 9 narrative reviews, 1 systematic review, and 1 basic science study.

Epidemiology

In North America and Western Europe, acute pericarditis is most often idiopathic or presumed due to a viral infection, and recurrence occurs in 15% to 30%.[1] Post–cardiac injury syndrome follows myocardial infarction (4%-5%), cardiac procedures (≈10% after ablation for atrial fibrillation), or cardiac procedures or operations (20%-30%) and is characterized by pericarditic or pleuritic chest pain, fever, pericardial or pleural rubs, pericardial effusion, or pleural effusion with an elevated C-reactive protein (CRP) level. Most episodes occur within a few weeks of the myocardial infarction, cardiac procedure, or cardiac surgery.[1,10-13] The incidence of recurrent pericarditis after an episode of post–cardiac injury syndrome is not well described. In much of the world, tuberculosis is the most common cause of pericarditis, with rates depending on the degree of endemicity.[14] For example, among persons in Africa with a pericardial effusion, tuberculosis is the cause in 65% to 70%.[14]

In addition, pericarditis can occur as a complication of malignancy, radiation therapy, nontuberculous bacterial infection (such as *Staphylococcus* or *Streptococcus*), chronic kidney failure, or an underlying systemic autoimmune disease.[15] Among patients with a malignant pericardial effusion, the most common causes are lung (≈40%), breast (≈25%), and hematologic (≈20%) malignancies.[1] Limited data are available, but pericarditis may occur in up to 20% of patients with systemic lupus erythematosus (SLE).[16,17] Acute pericarditis is less common in patients with rheumatoid arthritis, although 30% to 50% may have asymptomatic pericardial effusions.[15]

Pathophysiology

The parietal pericardium contains an outer fibrous sac and an inner serosal lining consisting of a single layer of mesothelial cells contiguous with the visceral pericardium (or epicardium) (**Figure 1**A). Normal pericardium is less than 1 mm in thickness and contains less than 50 mL of serous fluid, which is an ultrafiltrate of plasma. Typically, scant blood vessels are found within the parietal pericardium.[18] In response to an insult, such as a viral infection or direct cardiac injury, vascular permeability of the pericardium increases with fluid exudation and mesothelial cell desquamation followed by formation of granulation tissue, fibroblast proliferation, and newly formed blood vessels within the pericardium.[2,18]

Normal pericardial thickness approaches the limits of spatial resolution for cardiac imaging modalities and may not be visualized or else appears as a thin, linear structure. Therefore, the pericardium is often more readily visualized when it is abnormally thickened or inflamed. Any evidence of pericardial neovascularization, such as with retention of iodinated or gadolinium-based contrast, is generally pathologic.[11,19]

Recurrent pericarditis with an inflammatory phenotype (eg, elevated CRP level), usually represents an abnormal innate immune response, with an inappropriate activation of the NLRP3 inflammasome, a multiprotein complex that forms in response to infectious pathogens or tissue damage. The NLRP3 inflammasome complex activates caspase-1 dependent release of proinflammatory cytokines that can cause an autoinflammatory cycle leading to recurrent pericarditis, whereas inhibiting the NLRP3 inflammasome or downstream cytokines attenuates this response (Figure 1B).[20]

Clinical Presentation and Diagnosis

Acute pericarditis is diagnosed if 2 or more of the following 4 findings are present: nonischemic chest pain that is typically sharp, pleuritic, and worse when supine (≈90%); electrocardiographic (ECG) changes characterized by new widespread ST-segment elevation and PR-segment depression (≈25%-50%); a new or worsening pericardial effusion (≈60%) that is most often small; or a pericardial friction rub, which can be auscultated in less than 30% of cases.[1,21] A pericardial friction rub is high-pitched, may be transient, and is typically triphasic and heard best with the patient leaning forward (**Audio**). A detailed history regarding the quality of the chest pain is essential (eg, sharp, pleuritic, and changes with position); J-point elevation should not be mistaken as ECG changes of pericarditis; and epicardial fat observed on echocardiography should be distinguished from pericardial fluid (**Figure 2**). Unlike patients with acute pericarditis, those with recurrent pericarditis may be less likely to have characteristic ECG changes or a new or worsening pericardial effusion. In both acute and recurrent pericarditis, supportive findings include elevated inflammatory markers, including erythrocyte sedimentation rate and CRP level. Specifically, some clinical trials of patients with recurrent pericarditis have required a CRP level greater than 10 mg/L for inclusion.[22,23]

An appreciation of other supportive signs and symptoms also helps prevent a delay in diagnosis. Some patients with pericarditis may have a prominent cough or associated dyspnea. In addition,

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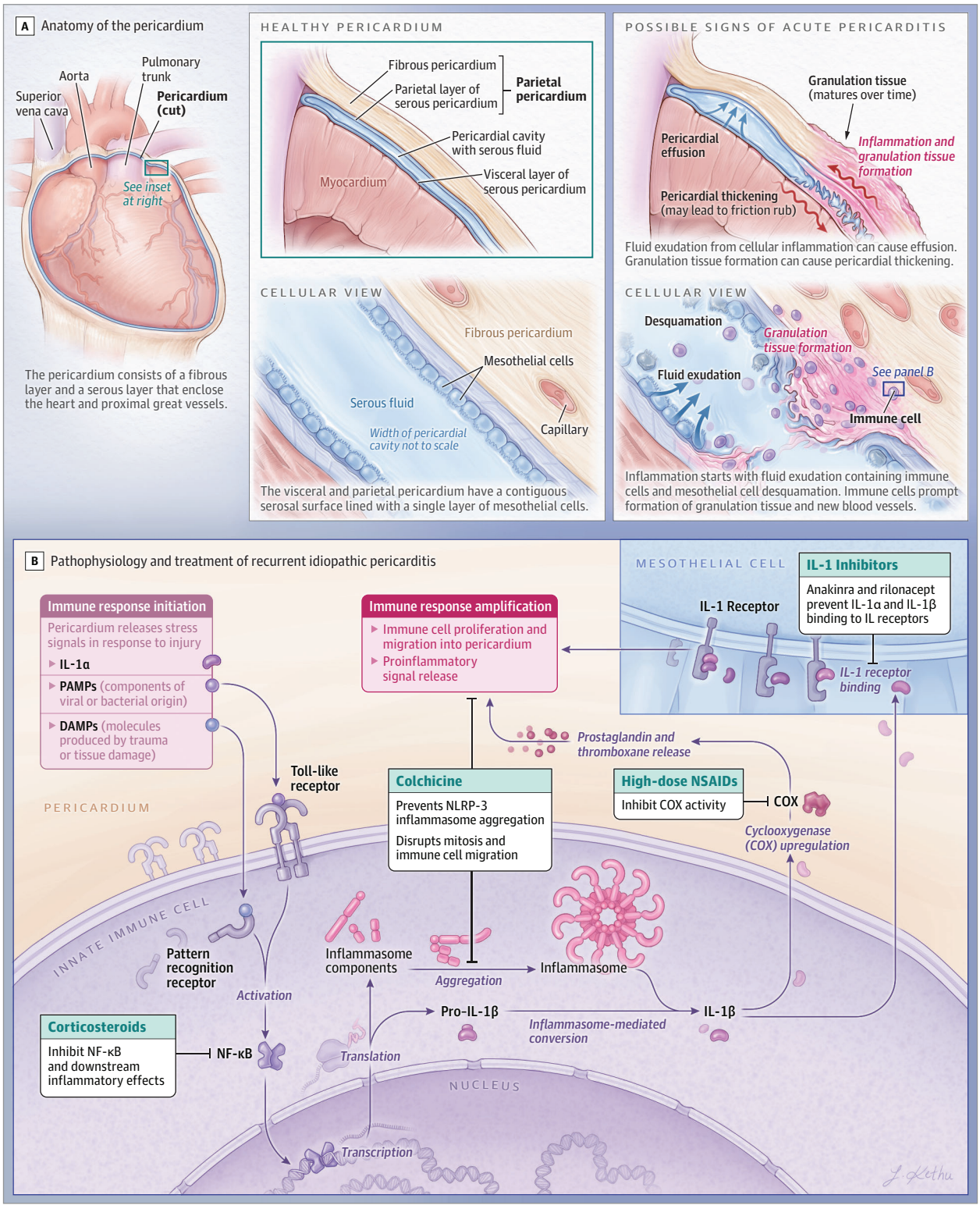
Figure 1. Anatomy of the Pericardium and Pathophysiology of Recurrent Idiopathic Pericarditis



A, Normal pericardium is less than 1 mm thick and contains less than 50 mL of fluid between the serosal layers. B, After recognition of endogenous danger signals such as from infectious pathogens or tissue damage (pathogen-associated molecular patterns [PAMPs] or damage-associated molecular patterns [DAMPs]), activation of toll-like receptors leads to formation of the inflammasome complex. The inflammasome then activates release of proinflammatory cytokines that drive the autoinflammatory cycle of recurrent pericarditis. Many therapeutics in pericarditis inhibit downstream consequences of this innate immune system activation of the inflammasome. IL indicates interleukin; NF-κB, nuclear factor κB; NSAID, nonsteroidal anti-inflammatory drug.

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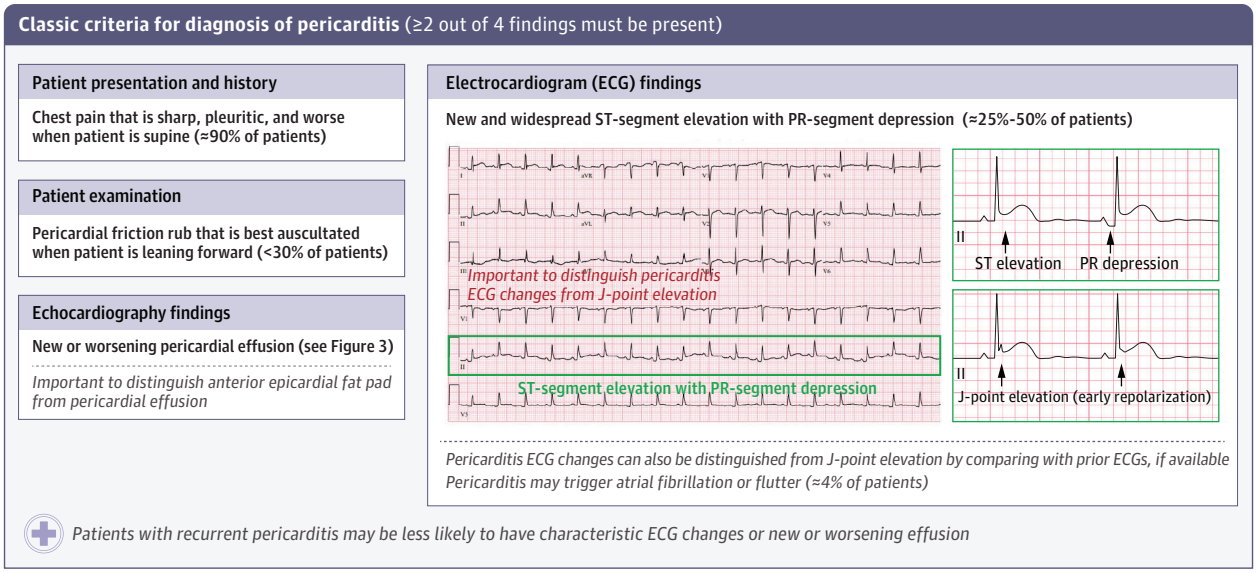
Figure 2. Diagnostic Approach to Pericarditis



Pericarditis is most often diagnosed when typical chest pain occurs with either electrocardiographic changes of new and widespread ST-segment elevation with PR-segment depression (except in aVR and often V_1), a new or worsening pericardial effusion, or a pericardial friction rub. In patients with a history of pericarditis, typical pericarditis chest pain with elevated C-reactive protein level is compatible with a recurrence. Cardiac magnetic resonance imaging is most often obtained in patients with a history of known or suspected recurrent pericarditis.

many patients may have systemic symptoms of fatigue and a low-grade fever, and these patients are more likely to have elevated levels of inflammatory markers, a neutrophilic leukocytosis with an absolute neutrophil count greater than the patient's baseline, and an elevated neutrophil to lymphocyte ratio.[24] Moreover, pericarditis can trigger an atrial tachyarrhythmia, and approximately 4% of patients with acute pericarditis present with atrial fibrillation or flutter.[25]

Patients with acute pericarditis should be assessed for risk factors for tuberculosis, associated malignancies, a known or suspected systemic autoimmune disease, and family history of pericarditis. In tuberculous pericarditis, patients generally present with typical pericarditis symptoms, but other common symptoms include cough, weight loss, fever, and night sweats.[1] In general, acute pericarditis is an unusual initial presenting symptom for an autoimmune disease such as SLE, because other disease manifestations typically predate pericarditis.[15] For patients with rheumatoid arthritis and systemic sclerosis, pericardial involvement more commonly presents as an asymptomatic pericardial effusion (30%-50%), instead of active pericarditis.[15] A family history of pericarditis may prompt a genetic evaluation, although the yield in assessing for monogenetic diseases such as familial Mediterranean fever is low.[26]

Laboratory Assessment

Among patients with acute idiopathic or viral pericarditis, a majority (78%) have an elevated CRP level, defined as greater than 3 mg/L. Potential causes for an initially normal CRP level in patients with acute pericarditis include an early clinical presentation (34%) or treatment with NSAIDs, colchicine, or corticosteroids (50%).[27]

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To evaluate for other causes of chest pain such as myocardial ischemia and for possible concomitant myocarditis, levels of cardiac troponin should be measured. In patients with acute pericarditis who have an elevated troponin level, most (80%) do not have left ventricular dysfunction at presentation. For individuals with acute pericarditis who have left ventricular dysfunction, a majority (85%) have left ventricular recovery by 12 months.[28] Patients with acute pericarditis who have an elevated cardiac troponin level but no left ventricular impairment have myopericarditis; their care management is the same as that for those with acute idiopathic or viral pericarditis, and an elevated troponin level is not a negative prognostic marker in this setting.[28]

Patients at risk for tuberculosis (such as those who live in or have immigrated from endemic areas; are unhoused; have experienced current or past imprisonment; or have immunocompromised status, including HIV infection) should be tested for tuberculosis.[14] Results of antinuclear antibody tests should be evaluated only when other signs or symptoms such as those for polyarticular arthritis suggest a systemic autoimmune disease, because low-level titers of antinuclear antibodies are common and nonspecific in patients with recurrent idiopathic pericarditis.[29]

For patients with acute pericarditis, pericardiocentesis is performed for overt or developing pericardial tamponade (see below) or when a bacterial, tuberculous, or a malignant cause of a pericardial effusion is suspected (**Video**). Assessment of pericardial fluid includes cell count, Gram stain and cultures, and cytology, although other tests are indicated in specific clinical scenarios (eg, triglyceride levels in patients with suspected chylous effusion). Cytology has a low sensitivity for pericarditis associated with malignancy, because approximately 25% of pericardial effusions with a benign cytologic interpretation may be due to an underlying neoplasm.[30] In addition, the Light criteria, a tool routinely used to assess pleural fluid, should not be applied to pericardial fluid because normal pericardial fluid is classified as exudative.[31]

Cardiac Imaging

All patients with suspected acute pericarditis should have echocardiography to assess for a thickened and hyperechoic pericardium, evaluate for a pericardial effusion, and define the hemodynamic consequences of pericardial pathology.[32,33] If echocardiography is not available, point-of-care ultrasound can identify a hemodynamically significant pericardial effusion, which may be characterized by diastolic collapse of the right ventricle. A chest radiograph is routinely obtained to evaluate for underlying causes of acute pericarditis such as tuberculosis or malignancy, but an increased cardiothoracic ratio occurs only with pericardial effusions exceeding 300 mL.[1]

Pericardial effusions are characterized according to their location and size, although the hemodynamic impact is primarily due to the rapidity of pericardial fluid accumulation rather than total volume. When a pericardial effusion develops rapidly, there has not been time for a compensatory increase in pericardial compliance. Pericardial tamponade can result, which is characterized by a precipitous increase in pericardial pressure with diastolic chamber collapse, severe impairment in diastolic filling, and a substantial reduction in stroke volume.[33] Clinical signs of tamponade include compensatory tachycardia, elevated jugular venous pressure, hypotension, and pulsus paradoxus (an inspiratory decrease in systolic arterial pressure of >10 mm Hg during normal breathing).[1] Patients with effusive constrictive pericarditis (defined classically as constrictive pathophysiology and a persistently elevated right atrial pressure following pericardiocentesis for tamponade) characteristically have a highly inflamed visceral pericardium.[34]

For patients with acute and recurrent pericarditis, the extent of neovascularization correlates with the severity of inflammation. Most often obtained in the setting of recurrent pericarditis, cardiac magnetic resonance imaging (CMR) demonstrating retention of gadolinium-based contrast within the pericardium reflects this ingrowth of blood vessels.[19] Given the minimal vascularity of normal pericardium, late gadolinium contrast enhancement (LGE) is an abnormal finding that must be interpreted together with the clinical setting, because it can be present in 44.1% of patients with prior cardiac surgery who have no signs or symptoms of pericarditis.[35] A patient with extensive pericardial edema and LGE on CMR has active pericarditis, a thickened pericardium and no LGE indicates no active inflammation and represents a chronic stage of the disease (**Figure 3**).[36]

Treatment and Prevention of Recurrence

Admission to the hospital for symptom management (eg, pain and shortness of breath) and hemodynamic monitoring can be considered for patients with acute pericarditis and a fever, symptoms developing over several days without a clear onset, a large pericardial effusion (>2.0 cm) or cardiac tamponade, a lack of response to previous treatment with NSAIDs, or for those with a suspected malignancy.[1] In the setting of certain diseases, such as tuberculosis and uremia, treatment is directed at the underlying cause. However, in North America and Western Europe—where the main causes of pericarditis are idiopathic, viral, and post–cardiac injury syndrome—treatment focuses on reducing symptoms and the number and severity of pericarditis flares.

NSAIDs

In acute pericarditis, despite the lack of randomized trial data in patients with idiopathic disease, NSAIDs are typically used to provide pain relief, starting at a high dose (eg, ibuprofen [1600-2400 mg/d] or aspirin [650-1000 mg 3 times a day]) and tapering the dose once chest pain has resolved and levels of inflammatory markers have normalized. Naproxen is also used, although fewer data are available compared with ibuprofen or aspirin. Gastroprotection with a proton pump inhibitor is recommended for patients taking high-dose NSAIDs.[1]

Colchicine

Many randomized trials in pericarditis have been performed evaluating colchicine added to standard NSAIDs (**Table 1**). Colchicine was first investigated for treatment of acute pericarditis nearly 40 years ago due to its efficacy in preventing recurrent polyserositis of familial Mediterranean fever.[37] In the 2013 ICAP (Investigation on Colchicine for Acute Pericarditis) study of 240 patients with acute pericarditis, development of incessant or recurrent pericarditis occurred in 16.7% of patients who received colchicine (at a dose of 0.5 mg twice daily for 3 months for patients weighing >70 kg or 0.5 mg once daily for patients weighing ≤70 kg) compared with 37.5% who received placebo.[38] Therefore, a 3-month course of colchicine is recommended for acute idiopathic pericarditis to prevent recurrence.[1]

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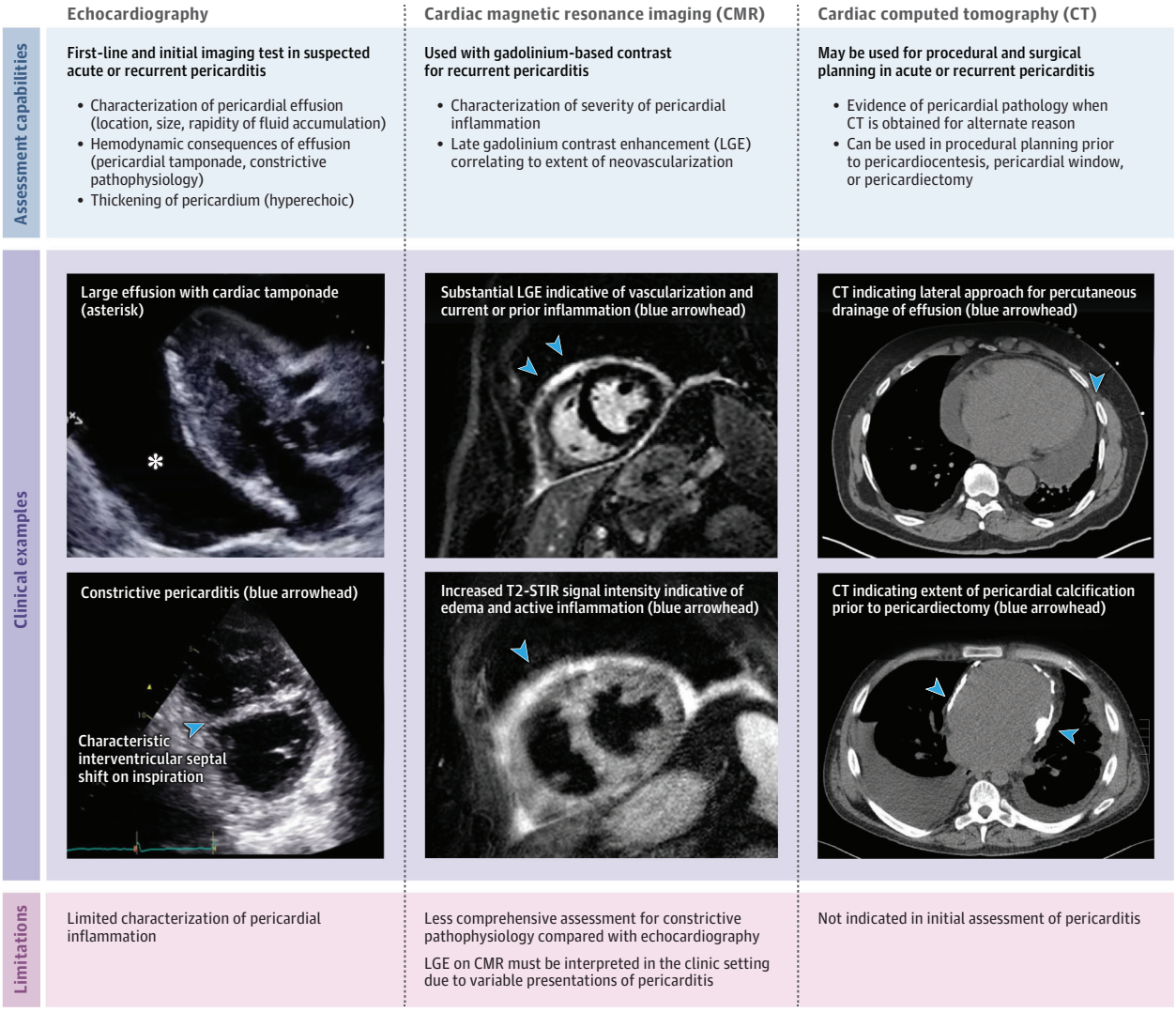
Figure 3. Imaging Assessment of Pericarditis



Echocardiography is the initial test to assess for a pericardial effusion and the hemodynamic consequences of pericardial pathology. The strength of cardiac magnetic resonance imaging is in characterizing pericardial inflammation, and cardiac computed tomography is generally reserved for procedural and surgical planning. T2-STIR indicates T2-weighted imaging with short tau inversion recovery.

Table 1. Pivotal Placebo-Controlled Randomized Clinical Trials of Colchicine in Pericarditis

	ICAP (n = 240)[37]	COPPS-2 (n = 360)[14]	CORP (n = 120)[3]	CORP-2 (n = 240)[4]
Cause of pericarditis, %	Idiopathic: 77.1 PCIS: 20.0 Connective tissue disease: 2.9	Not applicable	Idiopathic: 81.7 PCIS: 5.8 Connective tissue disease: 12.5	Idiopathic: 82.5 PCIS: 8.8 Connective tissue disease: 6.7
Pericarditis episodes	Acute	Prevention of PCIS	First recurrence	Multiple recurrences
Co-interventions, %	Aspirin or ibuprofen: 93.3 Prednisone: 6.7	None	Aspirin or ibuprofen: 92.5 Prednisone: 7.5	Aspirin or indomethacin: 93.3 Prednisone: 6.7
Primary end point	Incessant or recurrent pericarditis	PCIS	Recurrent pericarditis	Recurrent pericarditis
Follow-up, mo	18	18	18	18
Event rates (absolute risk reduction), %	37.5 vs 16.7 (absolute risk reduction, 20.8)	29.4 vs 19.4 (absolute risk reduction, 10.0)	55 vs 24 (absolute risk reduction, 31)	42.5 vs 21.6 (absolute risk reduction, 20.9)

Abbreviations: COPPS-2, Colchicine for Prevention of the Postpericardiotomy Syndrome and Postoperative Atrial Fibrillation; CORP, Colchicine for Recurrent Pericarditis; ICAP, Investigation on Colchicine for Acute Pericarditis; PCIS, post–cardiac injury syndrome.

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Table 2. Randomized Withdrawal Trials With IL-1 Blockers in Recurrent Pericarditis

	Anakinra (n = 21)[22]	Rilonacept (n = 61)[23]	Goflikicept (n = 20)[42]
Cause of recurrent pericarditis	Idiopathic	Idiopathic: 85% PCIS: 15%	Idiopathic
No. of prior recurrences for enrollment	At least 3 prior recurrences (mean, 6.8)	At least 2 prior recurrences (mean, 4.7)	At least 1 prior recurrence (45%, ≥3 recurrences)
Disease state at enrollment	Active (elevated CRP)	Active (elevated CRP)	Active: 41% Quiescent: 59%
Background therapy, %	Corticosteroids: 100 NSAIDs: 71.4 Colchicine: 85.7	Corticosteroids: 45.9 NSAIDs: 63.9 Colchicine: 86.9	Corticosteroids: 9.1[a] NSAIDs and/or colchicine: 90.9[a]
Tapering during run-in phase	NSAIDs stopped within 15 d; corticosteroids stopped by wk 7; colchicine discontinuation optional (57% continued)	Prespecified discontinuation of NSAIDs, colchicine, and corticosteroids by wk 10; median time to monotherapy 7-8 wk	NSAIDs and colchicine stopped on day 14 without tapering; corticosteroids stopped by wk 12
Primary end point	Recurrence (pericardial chest pain with CRP elevation)	Recurrence (pericardial chest pain with CRP elevation)	Recurrence (2 of the following: pericardial chest pain, CRP elevation, new or worsening pericardial effusion)
Randomized withdrawal follow-up	6 mo	Event driven; median time to recurrence with placebo was 8.6 wk	24 wk
Event rates, %	90.0 vs 18.2	74.2 vs 6.7	90.0 vs 0

Abbreviations: CRP, C-reactive protein; NSAID, nonsteroidal anti-inflammatory drug; PCIS, post–cardiac injury syndrome.

[a] For run-in period (n = 22).

In a randomized trial of 360 patients undergoing cardiac surgery, 19.4% who received colchicine (0.5 mg twice daily in patients ≥70 kg or 0.5 mg once daily in patients <70 kg; starting 48 to 72 hours before surgery and continued for 1 month) developed pericarditis compared with 29.4% assigned to placebo (absolute difference, 10.0% [95% CI, 1.1%-18.7%]; number needed to treat, 10).[11] Consequently, a 1-month course of colchicine can be considered after cardiac surgery, although gastrointestinal intolerance and drug-drug interactions may limit use.[1] To treat post–cardiac injury syndrome, guidelines recommend colchicine and aspirin or NSAIDs as in acute idiopathic pericarditis.[1]

In a trial of 120 patients with a first recurrence of pericarditis, subsequent recurrence occurred in 24% of patients who received colchicine and 55% who received placebo (absolute risk reduction, 0.31 [95% CI, 0.13-0.46]) (Table 1).[3] Among patients with a history of multiple recurrences, the CORP-2 (Colchicine for Recurrent Pericarditis) study of 240 patients demonstrated a recurrence rate of 21.6% in patients treated with colchicine (0.5 mg twice daily for 6 months for patients weighing >70 kg or 0.5 mg once daily for patients weighing ≤70 kg) compared with 42.5% in patients assigned to placebo (relative risk, 0.49 [95% CI, 0.24-0.65]; $P < .001$; number needed to treat, 5).[4] Overall, these data support colchicine as a medication for persons with acute or recurrent pericarditis, with a treatment duration of at least 6 months following a recurrence.[1] In addition, as noted, the treatment approach for idiopathic and post–cardiac injury syndrome is similar, even though few patients with post–cardiac injury syndrome have been included in clinical trials.[4,38] In general, colchicine is well tolerated, although gastrointestinal adverse effects such as nausea, vomiting, abdominal pain, and diarrhea may necessitate dose reduction or cessation in approximately 10% of patients.[1] Of note, colchicine has not been evaluated in randomized trials for other common causes of pericarditis, including tuberculous and autoimmune pericarditis.

Corticosteroids

Corticosteroids are frequently used to treat acute and recurrent pericarditis, although no randomized clinical trials evaluating corticosteroids have been performed. In observational studies, corticosteroids, especially at higher doses (eg, prednisone [1.0 mg/kg daily]), have been associated with an increased risk of recurrence of pericarditis.[39] Therefore, corticosteroids should only be prescribed at low to moderate doses (prednisone [0.25-0.5 mg/kg daily]) in patients who do not improve with NSAIDS and colchicine or have adverse outcomes with or contraindications to NSAIDs and colchicine. Additional indications for corticosteroids include a systemic autoimmune disease in which corticosteroids may be indicated for another indication, after cardiac surgery for symptoms not responsive to colchicine, and for patients with contraindications to high-dose NSAIDs (such as moderate to severe kidney failure, use of anticoagulation, or pregnancy after the 20th week of gestation). Low-dose prednisone (eg, [0.25-0.5 mg/kg daily]) and colchicine can be administered throughout pregnancy.[40] Although not recommended routinely for tuberculous pericarditis, corticosteroids can be considered for tuberculous constrictive pericarditis.[41] In severe kidney impairment, colchicine is contraindicated, and dialysis should be considered in uremic pericarditis.[1] Potential adverse effects of long-term corticosteroids include weight gain, hyperglycemia, osteoporosis, and adrenal insufficiency.[1]

Interleukin 1 Blockers

Based on clinical trial data (**Table 2**),[23,43] rilonacept is approved by the US Food and Drug Administration for treatment and prevention of recurrent pericarditis.[44] Interleukin 1 (IL-1) blockers such as anakinra and rilonacept are indicated for certain patients with multiple recurrent episodes of pericarditis who have colchicine-resistant or corticosteroid-dependent disease. Specifically, these therapies have demonstrated efficacy in patients who have an autoinflammatory phenotype, which is characterized by elevated CRP level (ie, >10 mg/L, the threshold used for inclusion in the clinical trials). With IL-1 blockers, the most common adverse events are injection site reactions (≈33%, predominantly mild or moderate in severity) and upper respiratory tract infections (20%-25%, also generally mild or moderate in severity).[23]

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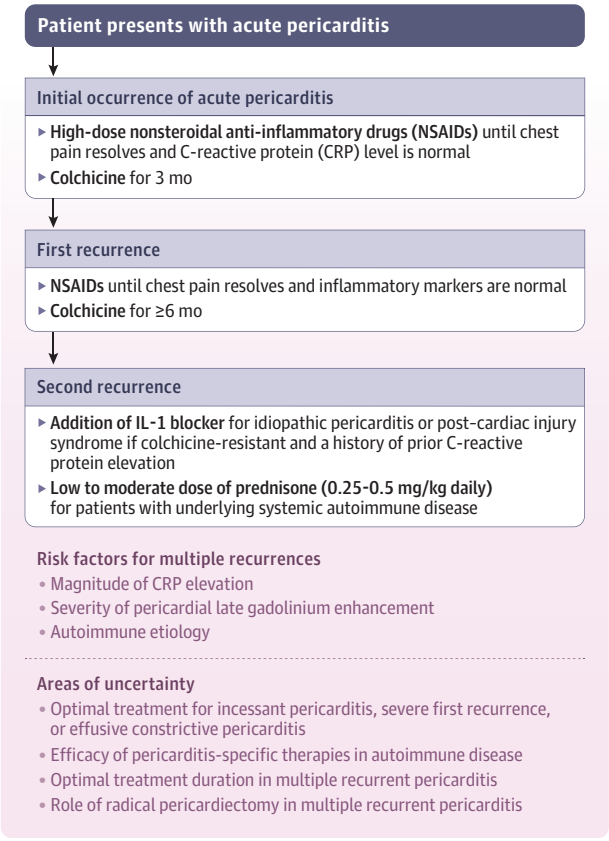
Figure 4. Treatment Approach in Pericarditis



In patients with acute pericarditis or a first recurrence, when idiopathic or due to post–cardiac injury syndrome, colchicine is added to NSAIDs. In patients with colchicine-resistant or corticosteroid-dependent pericarditis with a history of CRP elevation, interleukin 1 (IL-1) blockers are preferred to resolve active episodes and prevent recurrence. Risk factors may inform a longer duration of treatment to prevent recurrence.

In the AIRTRIP (Anakinra—Treatment of Recurrent Idiopathic Pericarditis) trial of 21 patients with idiopathic corticosteroid-dependent pericarditis and at least 3 prior recurrences, 9 of 10 patients (90%) had a recurrence of pericarditis after cessation of anakinra (an IL-1 receptor blocker), compared with recurrence in 2 of 11 patients (18%) who continued anakinra.[22] An international registry of 224 patients with colchicine-resistant and corticosteroid-dependent recurrent pericarditis reported that anakinra was associated with reduced recurrences, with lower rates of emergency department visits and hospitalizations.[45] In the RHAPSODY trial of patients with at least 2 prior recurrences of pericarditis, 23 of 31 patients (74%) had a recurrence after withdrawal of rilonacept compared with 2 of 30 patients (6.7%) who continued therapy.[23] Of note, patients taking corticosteroids were able to transition to rilonacept and discontinue corticosteroids in approximately 8 weeks.[46] These data suggest that patients treated with IL-1 blockers can be tapered off corticosteroids more rapidly (ie, decrease daily dose by 5 mg per week as long as the patient does not exhibit adrenal insufficiency), compared with slower tapering.[1] A randomized trial of 20 patients with idiopathic pericarditis and at least 1 prior recurrence reported that 9 of 10 patients randomized to withdrawal of goflikicept, another IL-1 blocker, had recurrent pericarditis compared with none of the 10 patients who continued goflikicept.[42]

Uncertainties in Treatment

Despite these advances in treatment, gaps remain in evidence-based care of many patients with pericarditis. First, avoidance of vigorous exercise for up to 3 months is often recommended for patients with acute pericarditis[1] because recurrences of pericarditis related to exercise have been reported, although rigorous studies are not available.[47] In addition, the best treatment approach for patients with incessant pericarditis or a severe first recurrence that does not improve with colchicine and NSAIDs is unclear. Given that the disease duration in multiple recurrent pericarditis can last for several years or longer, the optimal treatment duration with IL-1 blockers has not yet been defined. The optimal anti-inflammatory regimen for patients with effusive constrictive pericarditis is also uncertain. Furthermore, best treatment strategies for patients with pericarditis in the setting of an underlying autoimmune disease are not well defined. For example, neither colchicine nor IL-1 blockers have been well studied in pericarditis associated with SLE. However, in clinical practice, NSAIDs and colchicine are often used empirically for autoimmune-related pericarditis. Additionally, retrospective data have supported pericardiectomy in patients with refractory pericarditis pain,[48] but the optimal role for surgery with currently available anti-inflammatory therapy has not been defined. Last, despite the global burden of disease, few data are available regarding the management of tuberculous pericarditis.

Prognosis

After resolution of an acute flare of pericarditis, treatment should focus on reducing the risk of recurrent pericarditis and treating any underlying conditions (such as tuberculosis, autoimmune disorders, or dialysis for patients with uremia). A longer duration of therapy is indicated when the risk of recurrence is higher. After a first episode of idiopathic or viral pericarditis, recurrence may occur in 15% to 30% of patients; of these, 25% to 50% have subsequent flares. The majority of recurrences occur within 3 to 6 months, and recurrence beyond 12 months is unusual.[4,38] Accordingly, acute idiopathic or viral pericarditis and post–cardiac injury syndrome is typically treated for 3 months. The first recurrence is treated for 6 months, and longer treatment durations (often for several years) are indicated for multiple recurrences of pericarditis.[1]

Clinical risk factors such as an underlying autoimmune disease are associated with an approximately 50% increased risk of recurrent pericarditis.[6] Elevated inflammatory marker levels also have prognostic value. In patients with acute pericarditis, persistently elevated CRP levels after 1 week of therapy is associated with a higher risk of recurrence (hazard ratio, ≈2.4).[27] Similarly, among patients with an active flare of recurrent pericarditis, median time to clinical improvement, defined as symptom resolution with cessation of corticosteroids or immunomodulatory therapy, was 32 months in patients with CRP levels greater than 10 mg/L compared with 11 months in patients with CRP levels 10 mg/L or less.[49] The long-term extension of the RHAPSODY trial showed continued risk for pericarditis recurrence after 18 months of rilonacept.[50] Among the 8 patients who stopped rilonacept after 18 months, 6 (75%) had a recurrence at a median time of 11.8 weeks after treatment cessation.[50] The magnitude of pericardial LGE on CMR is also associated with further flares

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Table 3. Anti-Inflammatory Treatments for Pericarditis

Drug and dose	Duration	Tapering	Common adverse effects[a]
Acute or recurrent pericarditis			
Aspirin (500-1000 mg 3 times daily)	Until chest pain has resolved and CRP normalized (typically 1-2 wk for the initial episode) Weeks to months for recurrence	250- to 500-mg Decrease every 1-2 wk	Gastrointestinal (dyspepsia, peptic ulcer disease) Kidney (acute kidney injury) Cardiovascular (fluid retention, worsening of underlying hypertension)
Colchicine (0.5 to 1.2 mg daily) (<70 kg: 0.5 or 0.6 mg daily; >70 kg: 0.5 or 0.6 mg twice daily)	Acute: 3 mo Recurrence: ≥6 mo	Optional (eg, can decrease to once daily or every other day prior to discontinuation)	Gastrointestinal (diarrhea [23%], nausea, vomiting)
Ibuprofen (600-800 mg 3 times daily)	Until chest pain has resolved and CRP normalized (typically 1-2 wk for the initial episode) Weeks to months for recurrence	200- to 400-mg Decrease every 1-2 wk	Gastrointestinal (dyspepsia, peptic ulcer disease) Kidney (acute kidney injury, worsening of underlying hypertension)
Prednisone (0.25-0.5 mg/kg/d)	Weeks to months	Rapid dosage tapering to 25 mg/d Starting dose 15-25 mg: decrease 2.5 mg/d every 2-4 wk Starting dose <15 mg: decrease 1.25-2.5 mg/d every 2-6 wk Can taper more quickly (eg, 8 wk) in patients taking an IL-1 blocker	Cardiovascular (hypertension, fluid retention) Psychiatric (depression, agitation) Endocrine (cushingoid appearance, hyperglycemia, osteoporosis) Gastrointestinal (peptic ulcer, ulcerative esophagitis) Infections Myopathy Glaucoma
Recurrent pericarditis			
Anakinra (1-2 mg/kg/d, with a maximum dose of 100 mg subcutaneously daily)	At least 6-12 mo, with longer durations in multiple recurrent pericarditis	Optional (decrease by 100 mg per wk every month after several months of stability with daily therapy or decrease to every other day for 3 mo followed by half dose every other day for an additional 3 mo)[b]	Infection (39%; serious infection, 2%-3%; most commonly upper respiratory tract infections) Injection site reactions (71%)
Rilonacept (320 mg subcutaneously as a loading dose, followed by 160 mg weekly as a maintenance dose)	At least 6-12 mo, with longer durations in multiple recurrent pericarditis	Not investigated	Infection (34%-48%, most commonly upper respiratory tract infections) Injection site reactions (48%)

Abbreviations: CRP, C-reactive protein; IL-1, interleukin 1.

[a] UpToDate Lexidrug, https://www.uptodate.com/contents/table-of-contents/drug-information.

[b] The best approaches to tapering anakinra have not been compared.

in patients with recurrent pericarditis.[51,52] In an observational study of 365 patients with idiopathic post–cardiac injury syndrome or autoimmune pericarditis, significant pericardial LGE, defined as moderate or greater using a standardized assessment, was associated with a 40% higher recurrence risk after adjustment for other clinical variables.[6]

Patients with recurrent pericarditis generally have a disease course that lasts several months to years.[53] However, the clinical spectrum can vary from a single recurrence with minimal morbidity to a lifelong disease with substantial impairment in quality of life. Therefore, treatment regimens and durations are often individualized based on the number and severity of prior recurrences of pericarditis with consideration of clinical risk factors (**Figure 4** and **Table 3**).

Limitations

Several limitations should be noted. First, a formal literature quality assessment was not performed. Second, relevant articles may have been missed. Third, constrictive pathophysiology and subtypes of constrictive pericarditis were not discussed in depth. Fourth, long-term multicenter observational registry data of patients with pericarditis are lacking.

Conclusions

Acute pericarditis is a common cause of nonischemic chest pain. Tuberculosis is the leading cause of pericarditis in endemic areas and is treated with antitubercular therapy. In North America and Western Europe, pericarditis is typically idiopathic, develops after a viral infection, or develops following cardiac procedures or surgery. Treatment with NSAIDs and colchicine leads to a favorable prognosis in most patients, although 15% to 30% of patients develop recurrence. Patients with multiple recurrent pericarditis can have a disease duration of several years or more, are often treated with corticosteroids, and IL-1 blockers may be used for selected patients as steroid-sparing therapy.

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Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Kristin Walter, MD, at kristin.walter@jamanetwork.org.

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